4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2010-D-0283]

Guidance for Industry on Chemistry, Manufacturing, and Controls Postapproval Manufacturing Changes To Be Documented in Annual Reports; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled "CMC Postapproval Manufacturing Changes To Be Documented in Annual Reports." This guidance provides recommendations to holders of new drug applications (NDAs) and abbreviated new drug applications (ANDAs) regarding the types of changes to be documented in annual reports. Specifically, the guidance describes chemistry, manufacturing, and controls (CMC) postapproval manufacturing changes that FDA has determined will likely have a minimal potential to have an adverse effect on product quality and, therefore, should be documented by applicants in an annual report. (The guidance excludes positron emission tomography drug products.)

DATES: Submit either electronic or written comments on Agency guidances at any time.

ADDRESSES: Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

Submit electronic comments on the guidance to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Robert Iser, Office of Pharmaceutical Science, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 4178, Silver Spring, MD 20993-0002, 301-796-2400, Robert.Iser@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "CMC Postapproval Manufacturing Changes To Be Documented in Annual Reports." This guidance provides recommendations to holders of NDAs and ANDAs regarding the types of CMC postapproval manufacturing changes that FDA has determined will likely have a minimal potential to have an adverse effect on product quality, and therefore, should be documented by applicants in an annual report under § 314.70(d) (21 CFR 314.70(d)).

On June 25, 2010 (75 FR 36421), FDA announced the availability of the draft version of this guidance. The public comment period closed on September 23, 2010. A number of comments were received from the public, all of which the Agency considered carefully as it finalized the guidance and made appropriate changes. Any changes to the guidance were minor and made to clarify statements in the draft guidance.

In its September 2004 final report, “Pharmaceutical Current Good Manufacturing Practices (CGMPs) for the 21st Century – A Risk-Based Approach” (Pharmaceutical Product Quality Initiative,

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/QuestionsandAnswersonCurrentGoodManufacturingPracticescGMPforDrugs/ucm137175.htm), FDA stated that to keep pace with the many advances in quality management practices in manufacturing and to enable the Agency to more effectively allocate its limited regulatory resources, FDA would implement a cooperative, risk-based approach for regulating pharmaceutical manufacturing. As part of this approach, FDA determined that to provide the most effective public health protection, its CMC regulatory review should be based on an understanding of product risk and how best to manage this risk.

The number of CMC manufacturing supplements for NDAs and ANDAs has continued to increase over the last several years. In connection with FDA's Pharmaceutical Product Quality Initiative and its risk-based approach to CMC review, FDA has evaluated the types of changes that have been submitted in CMC postapproval manufacturing supplements and determined that many of the changes being reported present low risk to the quality of the product and do not need to be submitted in supplements.

Based on its risk-based evaluation, FDA developed a list (attached as an appendix to the guidance) to provide additional current recommendations to companies regarding some postapproval manufacturing changes for NDAs and ANDAs that may be considered to have a minimal potential to have an adverse effect on product quality, and, therefore, may be classified as a change to be documented in the next annual report (i.e., notification of a change after implementation) rather than in a supplement.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the Agency's current thinking on CMC postapproval manufacturing changes to be documented in annual reports. It does not create or confer any

rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit either electronic comments regarding this document to http://www.regulations.gov or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at http://www.regulations.gov.

III. Paperwork Reduction Act of 1995

This guidance contains collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information have been approved under OMB control number 0910-0758. This guidance also refers to the following previously approved collections of information: (1) The submission of supplements to FDA for certain changes to an approved application in accordance with § 314.70 and 21 CFR 314.71; (2) the submission of annual reports to FDA (Form FDA 2252) in accordance with § 314.81(b)(2) (21 CFR 314.81(b)(2)); (3) the submission of supplements to an approved ANDA for changes that require FDA approval; and (4) other post-marketing reports for ANDAs in accordance with 21 CFR 314.98(c), of which the estimate for annual reports is included under § 314.81(b)(2). FDA currently has OMB approval for these collections of information under OMB control number 0910-0001.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm or http://www.regulations.gov.

Dated: February 27, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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